REMARKS

Status of the Claims

Claims 23-25 and 27-30 are currently pending in the application. Claims 23-26 stand rejected. Claims 23, 24 and 25 have been amended. Claim 26 has been cancelled. All amendments and cancellations are made without prejudice or disclaimer. New claim 27 has been added. No new matter has been added by way of the present amendments. Specifically, the amendment to claims 23, 24 and 25 are generally clarifying amendments and are supported by the specification at, for instance, page 7, lines 3-14, page 14, line 21 to page 15, line 3, Example 10 and Table 10. New claim 27 is supported, for instance, at page 69, lines 16-19. New claims 28-30 are supported by original claims 23-25 and at least at page 10 of the specification. Reconsideration is respectfully requested.

Interview Summary

Applicants' representative wish to thank Examiner Wen and Examiner Gambrel for the personal interview conducted on May 20, 2008. Briefly, during the interview, all issues barring allowance of the present claims were discussed. Particularly, a set of claim amendments proposed by Applicants were reviewed by the Examiners and discussed. The Examiners indicated agreement that if the proposed amendments to the claims were submitted, they would most likely address all outstanding rejections and most likely place the claims in condition for allowance. Therefore, Applicants herein submit the proposed claim amendments for entry into the record and consideration by the Examiner. Reconsideration and allowance thereof are respectfully requested.

English Translation of Priority Application

It is noted that an English translation of applicant's priority application has not been submitted. (*See*, Office Action of February 28, 2008, at page 2, hereinafter, "Office Action"). However, as there is no intervening prior art and as the Examiner has not made a formal requirement for filing an English translation, no translation is submitted.

Specification

The Examiner states that Applicants should review the specification for spelling errors, the use of trademarks, embedded hyperlinks and/or other forms of browser-executable code. (*See*, *Id.* at page 3). The Examiner has not actually indicated the presence of any of these errors in the present specification. Although the specification has been reviewed for hyperlinks and trademarks, none were found. Thus, Applicants believe the specification properly complies with all Rules concerning disclosure.

Therefore, reconsideration and withdrawal of the objection to the specification are respectfully requested.

Claim Rejections Under 35 USC § 112, Second Paragraph

Claims 23-26 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. (*See*, Office Action, at page 4). Applicants respectfully traverse.

The Examiner states that the claims are missing essential steps needed to conduct the claimed methods, such as a contacting step, detecting step, measuring step, etc.

As discussed during the interview, claim 23 has been amended to clearly recite the steps of "contacting the specimen with" two separate antibodies and "detecting binding of antibodies (a) and (b)". The remaining independent claims have also been amended to include appropriate steps which define complete diagnostic method consistent with the objective stated in the preamble.

Accordingly, reconsideration and withdrawal of the indefiniteness rejection of claims 23-25 are respectfully requested.

Rejections Under 35 USC § 112, First Paragraph

Claims 25 and 26 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement support in the specification. (*See*, Office Action, at pages 4-8). Applicants respectfully traverse.

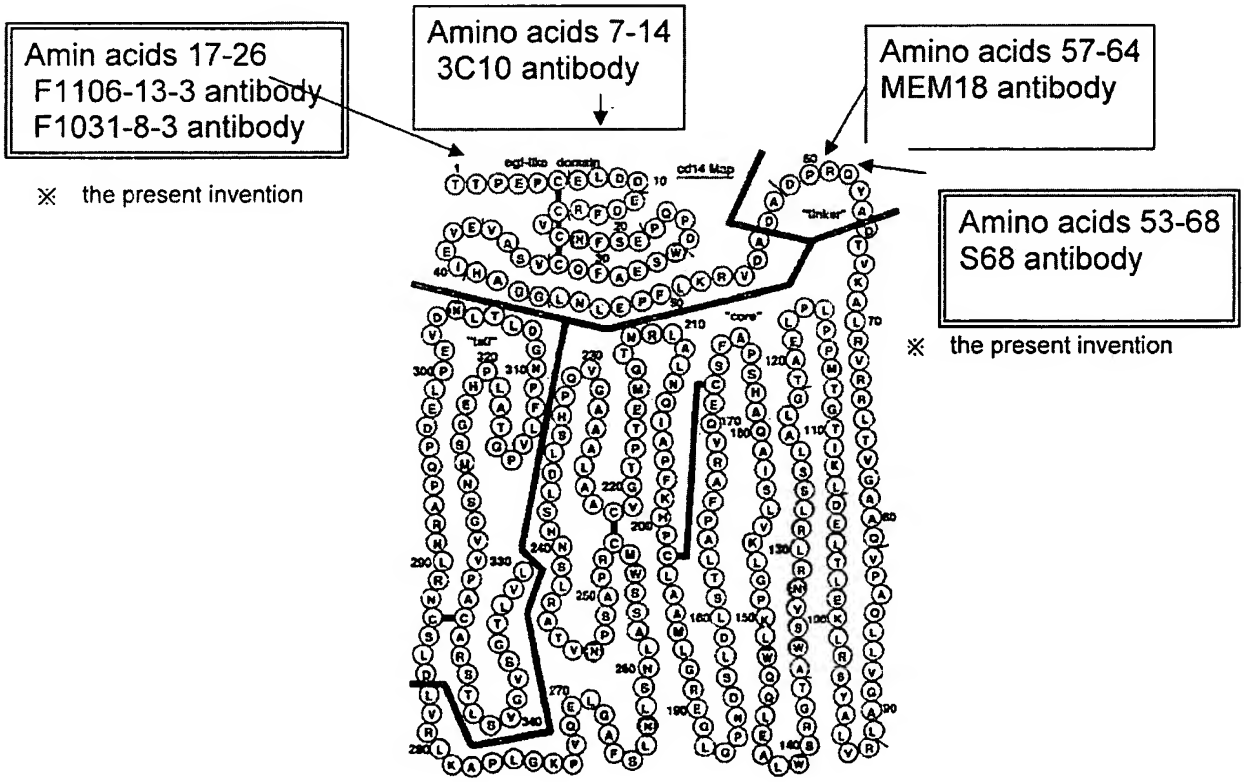
The Examiner states that at the time the present application was filed, sepsis was difficult to diagnose. The Examiner states that measurement of the level of CD14 does not indicate only sepsis. That is, the Examiner states that an elevated level of CD14 may be correlated with many diseases, such as sepsis, malaria, HIV and rheumatoid arthritis. The Examiner cites to Weinisch et al., *Clin. Exp. Immunol.*, 105:74-78, 1996, and Lien et al., *Blood*, 92:2084-2092, 1988 as evidence that levels of CD14 may be predictive of other diseases, not just sepsis. The Examiner also states that Applicants' claimed assay is not predictive of sepsis because the specification does not provide sufficient guidance on how to conduct or use the assay.

Applicants wish to first point out that both Weinisch et al. and Lien et al. measure only high-molecular-weight CD14, not low-molecular-weight CD14, as presently claimed. Thus, any

disclosure related to high-molecular-weight CD14 and diseases predicated on levels of the high-molecular-weight CD14 are inapposite to the presently claimed invention.

Furthermore, as discussed at the interview, and as hopefully more clearly reflected in the amended claims, the present invention is directed to diagnostic methods which are capable of specifically determining the presence of a "human low-molecular-weight CD14" (as more fully defined in the claims) that relies on sandwich immunoassay techniques. The sandwich immunoassay technique utilizes two different antibodies that bind to different epitopes that are both present on human low-molecular-weight CD14. The two different epitopes can be identified in the following diagram (discussed at the interview).

The primary structure and binding sites for antibodies of CD14



As also discussed at the interview, the detecting method using two antibodies recited in the claims do not both detect full-length native CD14. This is demonstrated by the data in the original specification (see Example 3-2 at pages 85-89, Example 10, and Table 10). Without wishing to be bound by any specific theory, this inability of the detecting method, using the two claimed antibodies, to detect full-length native CD14 is apparently a result of significant three-dimensional changes that occur when significant parts of the C–terminal part of CD14 is deleted from CD14. The present invention is based, in part, on the selection of antibodies that bind to a particular low-molecular-weight CD14, but which do not bind to full-length native CD14.

That is, the antibody recited in part (a) of claim 23, and similar parts of claims 24 and 25, binds only low-molecular-weight CD14, while the antibody of part (b) of these claims binds both high-molecular-weight CD14 and low-molecular-weight CD 14. As further explanation, it is noted that SEQ ID NO:2 recited in part (a) of the claims, corresponds to amino acid numbers 53-68 of human full length CD14. (*See*, specification, at page 24). SEQ ID NO:5 encodes human full-length CD14. (*See*, *Id.*). The antibody of (a) is similar to antibody S68 depicted in the above diagram, whereas the antibody of (b) is similar to antibody F1106-13-3. (*See*, *Id.* at pages 110-111). Meanwhile, the antibody recited in part (1) of claim 23, and similarly in the other claims 24 and 25, binds amino acids 316-328 of human CD14. (*See*, *Id.* at page 18).

The present inventors have also determined that there is a correlation between the presence of the claimed human low-molecular-weight CD14 and sepsis. (*See*, for instance, the present specification at Examples 10 and 11). The presently claimed method represents a novel and unobvious method for not only detecting low-molecular-weight CD14 (claims 23 and 24), but also for diagnosing sepsis (claims 25 – 27).

It is believed that the above explanation clearly demonstrates that the claims are based on sound scientific principles and reasoning and are fully supported by the specification.

Biological Deposit Issue

The Examiner states that the antibody F1025-3-1 is required to practice the invention. (*See*, Office Action, at page 9). The Examiner states that Applicants' biological deposit is not satisfactory.

Applicants assure that all requirements according to 37 C.F.R. §§ 1.801-1.809 will be satisfied.

Therefore, reconsideration and withdrawal of the enablement rejection of claim 25 are respectfully requested.

CONCLUSION

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Thomas J. Siepmann, PhD., Reg. No. 57,374, at the telephone number below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.147; particularly, extension of time fees.

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Respectfully submitted,

By _____ #32,881

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